

**AMENDMENTS TO THE CLAIMS**

Amend the claimed as follows:

Claims 1-89. (Cancelled)

90. (new) A compound having the following formula:



wherein:

Ar is a 1-(sulfonyl)-1H-indol-2-yl group;

the group -OR<sup>O</sup> is independently:

- (a) -OH;
- (b) an ether group; or:
- (c) an acyloxy group;

the bond marked  $\alpha$  is independently:

- (a) a single bond; or:
- (b) a double bond;

the bond marked  $\beta$  is independently:

- (a) a single bond; or:
- (b) a double bond;

each of R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup>, is independently a ring substituent and is:

- (a) H;
- (b) a monovalent monodentate substituent; or:

(c) a ring substituent which, together with an adjacent ring substituent, and together with the ring atoms to which these ring substituents are attached, form a fused ring;

and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

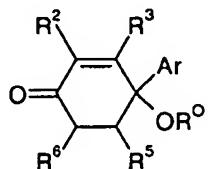
91. (new) A compound according to claim 90, wherein  $\alpha$  is independently a double bond and  $\beta$  is independently a double bond, and the compound has the following formula:



92. (new) A compound according to claim 90, wherein  $\alpha$  is independently a single bond and  $\beta$  is independently a single bond and the compound has the following formula:



93. (new) A compound according to claim 90, wherein  $\alpha$  is independently a single bond and  $\beta$  is independently a double bond, and the compound has the following formula:



(4)

94. (new) A compound according to claim 90, wherein said monovalent monodentate substituent is selected from:

hydroxy (-OH);

halo;

cyano (-CN);

carboxy (-COOH);

azido;

ester;

amino, including:

C<sub>1-7</sub>alkyl-amino;

amino-C<sub>1-7</sub>alkyl-amino;

C<sub>1-7</sub>alkyl, including:

halo-C<sub>1-7</sub>alkyl;

amino-C<sub>1-7</sub>alkyl;

carboxy-C<sub>1-7</sub>alkyl;

**STEVENS et al.**  
**U.S. National Phase of PCT/GB2002/005842**

hydroxy-C<sub>1-7</sub>alkyl;  
C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkyl;  
ether, including:  
    C<sub>1-7</sub>alkoxy;  
    halo-C<sub>1-7</sub>alkoxy;  
    amino-C<sub>1-7</sub>alkoxy;  
    carboxy-C<sub>1-7</sub>alkoxy;  
    hydroxy-C<sub>1-7</sub>alkoxy;  
    C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkoxy;  
acyl, including:  
    C<sub>1-7</sub>alkyl-acyl;  
    halo-C<sub>1-7</sub>alkyl-acyl;  
    amino-C<sub>1-7</sub>alkyl-acyl;  
    carboxy-C<sub>1-7</sub>alkyl-acyl;  
    hydroxy-C<sub>1-7</sub>alkyl-acyl;  
    C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkyl-acyl;  
C<sub>5-20</sub>aryl-acyl;  
C<sub>5-20</sub>aryl;  
thiol (-SH); and,  
thioether.

95. (new) A compound according to claim 90, wherein said monovalent monodentate substituent is selected from:

- OH;
- F, -Cl, -Br, -I;
- CN;
- COOH;
- N<sub>3</sub>;
- COOMe, -COOEt, -COOtBu, -COOPh, -COOCH<sub>2</sub>Ph;
  
- NH<sub>2</sub>, -NHMe, -NHEt, -NMe<sub>2</sub>, -NEt<sub>2</sub>;
- piperidino, morpholino, piperazino, N-methyl-piperazino;
- NH(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -NH(CH<sub>2</sub>)<sub>w</sub>-NHMe, -NH(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -NH(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;
  
- Me, -Et, -nPr, -iPr, -nBu, -iBu, -sBu, -tBu;
- CH<sub>2</sub>F, -CH<sub>2</sub>Cl, -CF<sub>3</sub>, -CCl<sub>3</sub>, -CF<sub>2</sub>CF<sub>3</sub>, -CH<sub>2</sub>CF<sub>3</sub>, -C(CF<sub>3</sub>)<sub>3</sub>;
- (CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>w</sub>-NHMe, -(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;
- (CH<sub>2</sub>)<sub>w</sub>-COOH;
- (CH<sub>2</sub>)<sub>w</sub>-OH;
- CH<sub>2</sub>Ph;
  
- OMe, -OEt, -OnPr, -OiPr, -OnBu, -OiBu, -OsBu, -OtBu;

STEVENS et al.  
U.S. National Phase of PCT/GB2002/005842

-OCH<sub>2</sub>F, -OCH<sub>2</sub>Cl, -OCF<sub>3</sub>, -OCCl<sub>3</sub>, -OCF<sub>2</sub>CF<sub>3</sub>, -OCH<sub>2</sub>CF<sub>3</sub>, -OC(CF<sub>3</sub>)<sub>3</sub>;  
-O(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -O(CH<sub>2</sub>)<sub>w</sub>-NHMe, -O(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -O(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
-O(CH<sub>2</sub>)<sub>w</sub>-COOH;  
-O(CH<sub>2</sub>)<sub>w</sub>-OH;  
-OCH<sub>2</sub>Ph;  
  
-C(=O)Me, -C(=O)Et, -C(=O)-nPr, -C(=O)-iPr, -C(=O)-nBu, -C(=O)-iBu,  
-C(=O)-sBu, -C(=O)-tBu;  
-C(=O)CH<sub>2</sub>F, -C(=O)CH<sub>2</sub>Cl, -C(=O)CF<sub>3</sub>, -C(=O)CCl<sub>3</sub>, -C(=O)CF<sub>2</sub>CF<sub>3</sub>,  
-C(=O)CH<sub>2</sub>CF<sub>3</sub>, -C(=O)C(CF<sub>3</sub>)<sub>3</sub>;  
-C(=O)(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -C(=O)(CH<sub>2</sub>)<sub>w</sub>-NHMe, -C(=O)(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>,  
-C(=O)(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
-C(=O)(CH<sub>2</sub>)<sub>w</sub>-COOH;  
-C(=O)(CH<sub>2</sub>)<sub>w</sub>-OH;  
-C(=O)CH<sub>2</sub>Ph;  
  
-Ph;

-SH;  
-SMe, -SEt, -SnPr, -S-iPr, -S-nBu, -S-iBu, -S-sBu, -S-tBu,  
-S-CH<sub>2</sub>-Ph, -S-Ph;

a thioether group derived from cysteine, homocysteine, glutathione, or a peptide comprising the sequence -Cys-(X)<sub>y</sub>-Cys-, where X is an amino acid, and y is an integer from 1 to 6;

wherein w is an integer from 1 to 7.

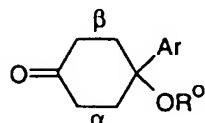
96. (new) A compound according to claim 90, wherein each of R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup>, is independently a ring substituent and is:

- (a) H; or:
- (b) a monovalent monodentate substituent.

97. (new) A compound according to claim 91, wherein each of R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup>, is independently a ring substituent and is:

- (a) H; or:
- (b) a monovalent monodentate substituent.

98. (new) A compound according to claim 90, wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup> and R<sup>6</sup> are -H:



(9)

99. (new) A compound according to claim 90, wherein R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup> and R<sup>6</sup> are -H; α is a double bond; and β is a double bond:



(11)

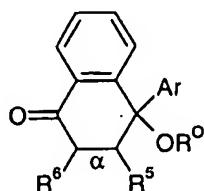
100. (new) A compound according to claim 90, wherein

(a) R<sup>2</sup> and R<sup>3</sup>, together with the ring atoms to which they are attached, form a fused ring; or

(b) R<sup>5</sup> and R<sup>6</sup>, together with the ring atoms to which they are attached, form a fused ring; or

(c) or both (a) and (b).

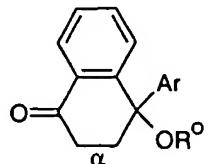
101. (new) A compound according to claim 99, wherein R<sup>2</sup> and R<sup>3</sup> form a fused benzene ring; and β is a double bond:



(14)

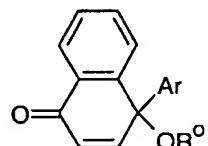
102. (new) A compound according to claim 101, wherein R<sup>5</sup> and R<sup>6</sup> do not also form a fused ring.

103. (new) A compound according to claim 99, wherein R<sup>2</sup> and R<sup>3</sup> form a fused benzene ring; β is a double bond; and R<sup>5</sup> and R<sup>6</sup> are -H:



(17)

104. (new) A compound according to claim 99, wherein R<sup>2</sup> and R<sup>3</sup> form a fused benzene ring; β is a double bond; R<sup>5</sup> and R<sup>6</sup> are -H; and α is a double bond:



(18)

105. (new) A compound according to claim 90, wherein R<sup>0</sup> is independently:

(a) -H;

(b) C<sub>1-7</sub>alkyl, C<sub>3-20</sub>heterocyclyl, or C<sub>5-20</sub>aryl; and is optionally substituted;

or:

(c) C<sub>1-7</sub>alkyl-acyl, C<sub>3-20</sub>heterocyclyl-acyl, or C<sub>5-20</sub>aryl-acyl; and is optionally substituted.

**STEVENS et al.**  
**U.S. National Phase of PCT/GB2002/005842**

106. (new) A compound according to claim 104, wherein R<sup>O</sup> is optionally substituted with one more of the following groups:

hydroxy (-OH);

halo;

carboxy (-COOH);

amino; and,

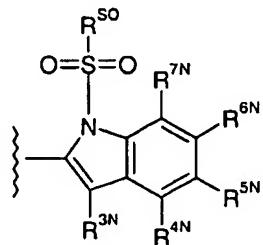
C<sub>5-20</sub>aryl.

107. (new) A compound according to claim 90, wherein R<sup>O</sup> is -H.

108. (new) A compound according to claim 91, wherein R<sup>O</sup> is -H.

109. (new) A compound according to claim 99, wherein R<sup>O</sup> is -H.

110. (new) A compound according to claim 90, wherein Ar is a group of the following formula:



wherein:

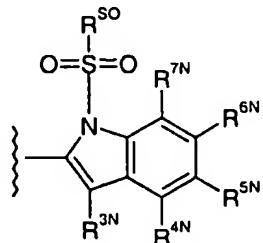
R<sup>SO</sup> is independently a sulfonyl substituent; and

each of  $R^{3N}$ ,  $R^{4N}$ ,  $R^{5N}$ ,  $R^{6N}$ , and  $R^{7N}$  is independently an indolyl substituent.

111. (new) A compound according to claim 110, wherein  $R^{SO}$  is  $C_{1-7}$ alkyl,  $C_{3-20}$ heterocyclyl, or  $C_{5-20}$ aryl; and is optionally substituted.

112. (new) A compound according to claim 110, wherein  $R^{SO}$  is  $C_{5-20}$ aryl; and is optionally substituted.

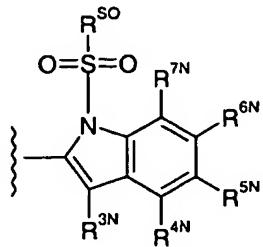
113. (new) A compound according to claim 99, wherein Ar is a group of the following formula:



wherein:

$R^{SO}$  is independently  $C_{5-20}$ aryl; and is optionally substituted; and each of  $R^{3N}$ ,  $R^{4N}$ ,  $R^{5N}$ ,  $R^{6N}$ , and  $R^{7N}$  is independently an indolyl substituent.

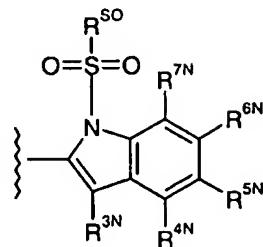
114. (new) A compound according to claim 104, wherein Ar is a group of the following formula:



wherein:

R<sup>SO</sup> is independently C<sub>5-20</sub>aryl; and is optionally substituted; and each of R<sup>3N</sup>, R<sup>4N</sup>, R<sup>5N</sup>, R<sup>6N</sup>, and R<sup>7N</sup> is independently an indolyl substituent.

115. (new) A compound according to claim 109, wherein Ar is a group of the following formula:



wherein:

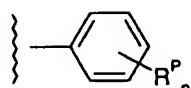
R<sup>SO</sup> is independently C<sub>5-20</sub>aryl; and is optionally substituted; and each of R<sup>3N</sup>, R<sup>4N</sup>, R<sup>5N</sup>, R<sup>6N</sup>, and R<sup>7N</sup> is independently an indolyl substituent.

116. (new) A compound according to claim 110, wherein R<sup>SO</sup> is phenyl or naphthyl; and is optionally substituted.

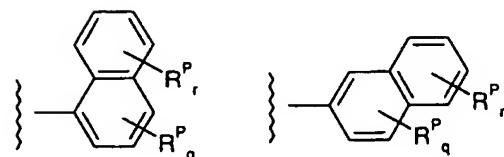
117. (new) A compound according to claim 110, wherein R<sup>SO</sup> is naphthyl; and is optionally substituted.

118. (new) A compound according to claim 110, wherein R<sup>SO</sup> is phenyl; and is optionally substituted.

119. (new) A compound according to claim 110, wherein R<sup>SO</sup> is selected from:



wherein p is an integer from 0 to 5, and each R<sup>P</sup> is a phenyl substituent;  
and



wherein q is an integer from 0 to 3; r is an integer from 0 to 4; and each R<sup>P</sup> is a naphthyl substituent.

120. (new) A compound according to claim 119, wherein each R<sup>P</sup> is independently selected from:

hydroxy (-OH);

halo;

cyano (-CN);

carboxy (-COOH);

azido;

ester;

amino, including:

amino-C<sub>1-7</sub>alkyl-amino;

C<sub>1-7</sub>alkyl, including:

halo-C<sub>1-7</sub>alkyl;

amino-C<sub>1-7</sub>alkyl;

carboxy-C<sub>1-7</sub>alkyl;

hydroxy-C<sub>1-7</sub>alkyl;

C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkyl;

ether, including:

C<sub>1-7</sub>alkoxy;

halo-C<sub>1-7</sub>alkoxy;

amino-C<sub>1-7</sub>alkoxy;

carboxy-C<sub>1-7</sub>alkoxy;

hydroxy-C<sub>1-7</sub>alkoxy;

C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkoxy;  
acyl, including:  
C<sub>1-7</sub>alkyl-acyl;  
halo-C<sub>1-7</sub>alkyl-acyl;  
amino-C<sub>1-7</sub>alkyl-acyl;  
carboxy-C<sub>1-7</sub>alkyl-acyl;  
hydroxy-C<sub>1-7</sub>alkyl-acyl;  
C<sub>5-20</sub>aryl-C<sub>1-7</sub>alkyl-acyl;  
C<sub>5-20</sub>aryl-acyl;  
C<sub>5-20</sub>aryl.

121. (new) A compound according to claim 119, wherein each R<sup>P</sup> is independently selected from:

-OH;  
-F, -Cl, -Br, -I;  
-CN;  
-COOH;  
-N<sub>3</sub>;  
-COOMe, -COOEt, -COOtBu, -COOPh, -COOCH<sub>2</sub>Ph;  
  
-NH<sub>2</sub>, -NHMe, -NHEt, -NMe<sub>2</sub>, -NEt<sub>2</sub>;

STEVENS et al.  
U.S. National Phase of PCT/GB2002/005842

piperidino, morpholino, piperazino, N-methyl-piperazino;  
-NH(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -NH(CH<sub>2</sub>)<sub>w</sub>-NHMe, -NH(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -NH(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
  
-Me, -Et, -nPr, -iPr, -nBu, -iBu, -sBu, -tBu;  
-CH<sub>2</sub>F, -CH<sub>2</sub>Cl, -CF<sub>3</sub>, -CCl<sub>3</sub>, -CF<sub>2</sub>CF<sub>3</sub>, -CH<sub>2</sub>CF<sub>3</sub>, -C(CF<sub>3</sub>)<sub>3</sub>;  
-(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>w</sub>-NHMe, -(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
-(CH<sub>2</sub>)<sub>w</sub>-COOH;  
-(CH<sub>2</sub>)<sub>w</sub>-OH;  
-CH<sub>2</sub>Ph;  
  
-OMe, -OEt, -OnPr, -OiPr, -OnBu, -OiBu, -OsBu, -OtBu;  
-OCH<sub>2</sub>F, -OCH<sub>2</sub>Cl, -OCF<sub>3</sub>, -OCCl<sub>3</sub>, -OCF<sub>2</sub>CF<sub>3</sub>, -OCH<sub>2</sub>CF<sub>3</sub>, -OC(CF<sub>3</sub>)<sub>3</sub>;  
-O(CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -O(CH<sub>2</sub>)<sub>w</sub>-NHMe, -O(CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>, -O(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
-O(CH<sub>2</sub>)<sub>w</sub>-COOH;  
-O(CH<sub>2</sub>)<sub>w</sub>-OH;  
-OCH<sub>2</sub>Ph;  
  
-C(=O)Me, -C(=O)Et, -C(=O)-nPr, -C(=O)-iPr, -C(=O)-nBu, -C(=O)-iBu,  
-C(=O)-sBu, -C(=O)-tBu;  
-C(=O)CH<sub>2</sub>F, -C(=O)CH<sub>2</sub>Cl, -C(=O)CF<sub>3</sub>, -C(=O)CCl<sub>3</sub>, -C(=O)CF<sub>2</sub>CF<sub>3</sub>,  
-C(=O)CH<sub>2</sub>CF<sub>3</sub>, -C(=O)C(CF<sub>3</sub>)<sub>3</sub>;

-C(=O) (CH<sub>2</sub>)<sub>w</sub>-NH<sub>2</sub>, -C(=O) (CH<sub>2</sub>)<sub>w</sub>-NHMe, -C(=O) (CH<sub>2</sub>)<sub>w</sub>-NMe<sub>2</sub>,  
-C(=O)(CH<sub>2</sub>)<sub>w</sub>-NEt<sub>2</sub>;  
-C(=O) (CH<sub>2</sub>)<sub>w</sub>-COOH;  
-C(=O) (CH<sub>2</sub>)<sub>w</sub>-OH;  
-C(=O)CH<sub>2</sub>Ph;  
  
-Ph;

wherein w is an integer from 1 to 7.

122. (new) A compound according to claim 119, wherein each R<sup>P</sup> is independently selected from: -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt.

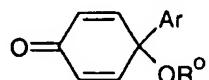
123. (new) A compound according to claim 119, wherein each R<sup>P</sup> is independently selected from: -F, -Me, -OMe.

124. (new) A compound according to claim 120, wherein each of R<sup>3N</sup>, R<sup>4N</sup>, R<sup>5N</sup>, R<sup>6N</sup>, and R<sup>7N</sup> is independently -H, or as defined for R<sup>P</sup>.

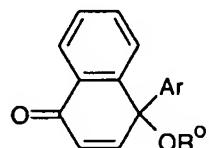
125. (new) A compound according to claim 120, wherein each of R<sup>3N</sup>, R<sup>4N</sup>, R<sup>5N</sup>, R<sup>6N</sup>, and R<sup>7N</sup> is independently selected from:  
-H, -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt.

126. (new) A compound according to claim 120, wherein each of  $R^{3N}$ ,  $R^{4N}$ ,  $R^{6N}$ , and  $R^{7N}$  is -H.

127. (new) A compound selected from compounds having the following formulae and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof:



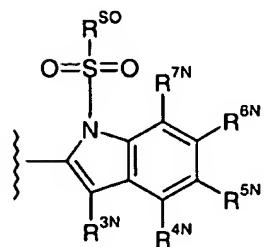
(11)



(18)

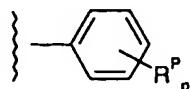
wherein  $R^o$  is -H;

wherein Ar is a group of the following formula:

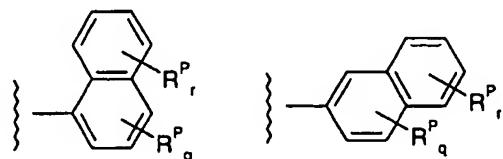


wherein:

$R^{SO}$  is selected from:



wherein p is an integer from 0 to 5, and each  $R^P$  is a phenyl substituent; and



wherein q is an integer from 0 to 3; r is an integer from 0 to 4; and each  $R^P$  is a naphthyl substituent;

and wherein:

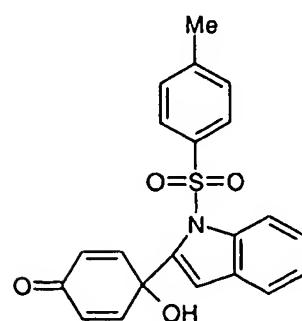
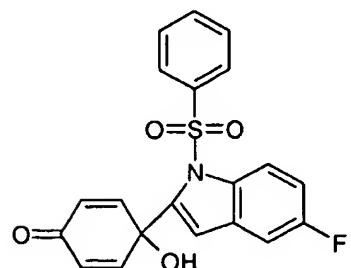
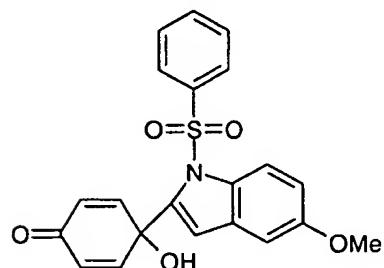
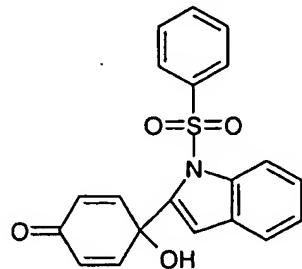
each of  $R^{3N}$ ,  $R^{4N}$ ,  $R^{5N}$ ,  $R^{6N}$ , and  $R^{7N}$  is independently an indolyl substituent.

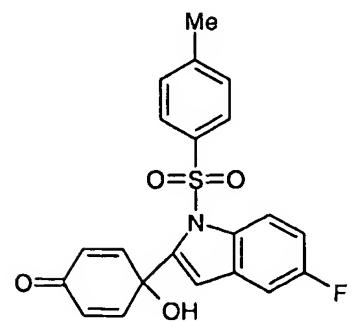
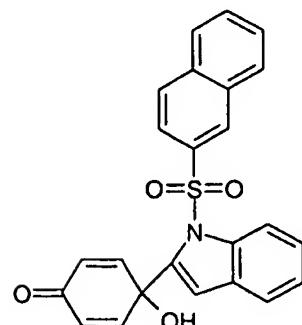
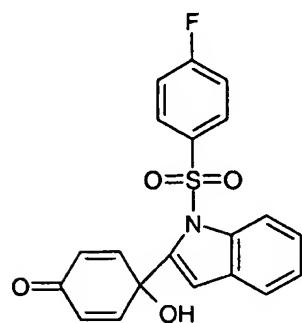
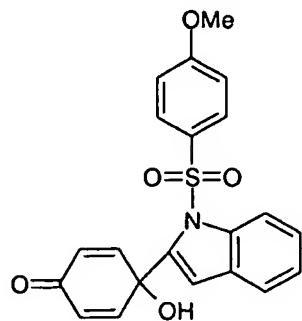
128. (new) A compound according to claim 127, wherein:

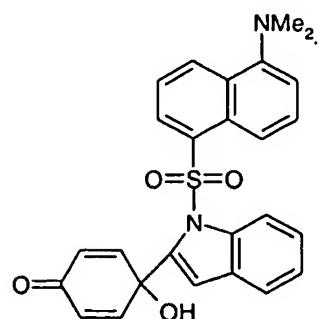
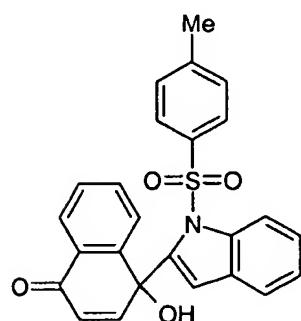
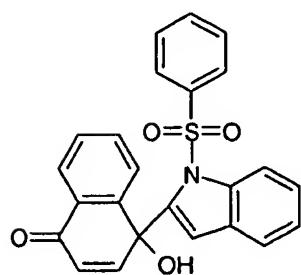
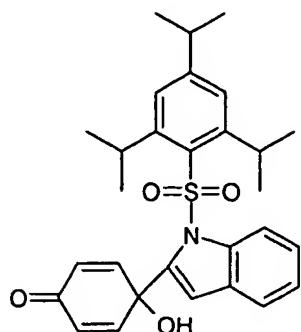
each  $R^P$  is independently selected from: -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt; and

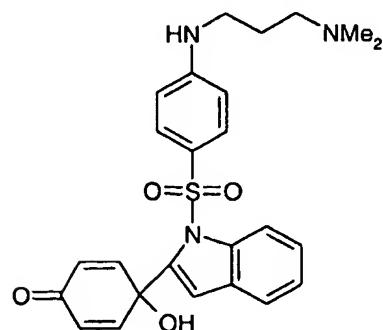
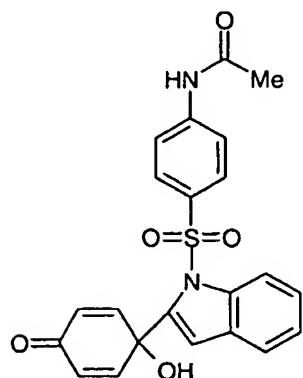
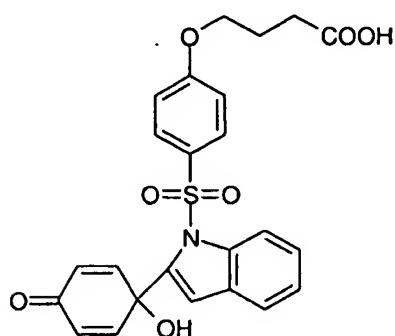
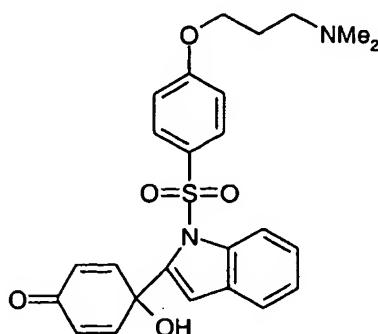
each of  $R^{3N}$ ,  $R^{4N}$ ,  $R^{5N}$ ,  $R^{6N}$ , and  $R^{7N}$  is independently selected from: -H, -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt.

129. (new) A compound selected from the following compounds and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof:









130. (new) A composition comprising a compound according to claim 90 and a pharmaceutically acceptable carrier or diluent.

131. (new) A method for the treatment of a proliferative condition comprising administering to a subject suffering from said condition a therapeutically-effective amount of a compound according to claim 90.

132. (new) A method for the treatment of cancer comprising administering to a subject suffering from said cancer a therapeutically-effective amount of a compound according to claim 90.

133. (new) A method for the treatment of colon cancer or renal cancer comprising administering to a subject suffering from said cancer a therapeutically-effective amount of a compound according to claim 90.

134. (new) A method for the treatment of a condition mediated by thioredoxin/thioredoxin reductase comprising administering to a subject suffering from said condition a therapeutically-effective amount of a compound according to claim 90.

c

135. (new) A method of inhibiting thioredoxin/thioredoxin reductase in a cell, *in vitro* or *in vivo*, comprising contacting said cell with an effective amount of according to claim 90.

136. (new) A method of regulating cell proliferation, *in vitro* or *in vivo*, comprising contacting a cell with an effective amount of a compound according to claim 90.

137. (new) A method of (a) inhibiting cell proliferation; (b) inhibiting cell cycle progression; (c) promoting apoptosis; or (d) a combination of one or more of these, *in vitro* or *in vivo*, comprising contacting a cell with an effective amount of a compound according to claim 90.